REMARKS

Claim Amendments

Upon entry of the foregoing amendment, claims 1-2, 15-17, 24, and 27 are pending in the application. Claims 1-2, 15, 24, and 27 have been amended. Claims 3-14, 18-23, 25-26, and 38-30 have been cancelled without prejudice or disclaimer to the subject matter therein. Applicants reserve the right to pursue the subject matter of the cancelled claims in one or more divisional and/or continuation applications. Support for the amendments to the claims can be found throughout the specification and in the claims as originally filed. *See, e.g.*, paragraphs [0059], [0066], [0073], [0079], Example 1, and original claim 13. Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter.

Specification Amendments

Applicants have amended the specification to include SEQ ID NOs. Applicants respectfully request entry of the amendment to the specification and submit that the amendment does not constitute new matter.

Objections to the Specification

The specification has been objected to under 37 C.F.R.§ 1.821(d) as allegedly failing to refer to a sequence by use of its sequence identifier preceded by "SEQ ID NO:." As per the Examiner's suggestion, Applicants have amended the specification to recite SEQ ID NOs. In view of the foregoing, Applicants respectfully submit that this objection is *moot*.

Claim Objections

Claims 4-6 have been objected under 37 C.F.R. § 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Without acquiescing to the correctness of the Examiner's objection, Applicants have canceled claims 4-6 without prejudice or disclaimer to the subject matter therein. In view of the foregoing, Applicants respectfully submit that this objection is *moot*.

Claim rejections – 35 U.S.C. § 112, second paragraph

Claims 1-6, 10-18, 20-21, 24, 27, and 30 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants respectfully disagree and traverse this rejection.

Claim 1 stands rejected over the recitation "an oilseed rape." Applicants have amended claim 1 to delete the term "an oilseed rape," thereby rendering this rejection *moot.*

Claims 1 and 10 stands rejected over the recitation "homologous gene." Applicants have amended claim 1 to delete the term "homologous gene" and cancelled claim 10, thereby rendering this rejection *moot.*

Claims 1, 10, 12, and 18 stands rejected over the recitation of "an *INDEHISCENT* gene from *Arabidopsis thaliana.*" Applicants have amended claim 1 to delete the term "an *INDEHISCENT* gene from *Arabidopsis thaliana,*" thereby rendering this rejection *moot.*

Claim 1 stands rejected over the recitation of "said 19 consecutive nucleotides" in parts (ii) and (iii). Applicants have amended claim 1 per the Examiner's suggestion and changed "19" to "200," thereby rendering this rejection *moot.*

Claim 1 stands rejected for allegedly omitting to recite "maintaining an agronomically relevant threshability" in the selection step. Applicants have amended claim 1 to include this feature in the selection step, thereby rendering the rejection *moot.*

Claim Rejection – 35 U.S.C. § 112, first paragraph (written description)

Claims 1-6, 10-18, 20-21, 24, 27, and 30 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully disagree and traverse this rejection.

Nonetheless, without acquiescing to the correctness of the rejection, Applicants have amended claims 1-2, 15, 24, and 27 and cancelled claims 2-6, 10-14, 18, 20-21, and 30. Furthermore, Applicants provide the following remarks.

The claims, as amended, are directed to a method of using a chimeric gene comprising a DNA region which, when transcribed, yields a double-stranded RNA molecule comprising a first and second RNA region, wherein the first RNA region comprises a nucleotide sequence of at least 200 consecutive nucleotides selected from the nucleotide sequence of SEQ ID NO: 1 other than a basic helix-loop-helix encoding region

and the second RNA region comprises a nucleotide sequence complementary to the 200 consecutive nucleotides of the first RNA region.

The specification provides (by definition) the complete sequence of SEQ ID NO: 1. Furthermore, the region encoding the basic helix loop helix from the INDEHISCENT gene of *Arabidopsis thaliana* is known in the art. *See, e.g.*, ¶¶ [0005], [0056], and [0059]. Applicants further submit that the specification describes specific nucleotide sequence fragments of SEQ ID NO: 1 (*e.g.*, at least 200, 500 consecutive nucleotides) encompassed by the claims and two homologues of SEQ ID NO: 1 (*e.g.*, SEQ ID NO: 2 and 3). *See* Specification at ¶¶ [0068], [0087]-[0088], and Figure 1. The specification also describes chimeric genes encoding dsRNA capable of reducing the expression of a gene involved in dehiscence zone and value margin development. *See* Specification at Example 1. Accordingly, Applicants submit that the specification provides the requisite structural and functional parameters of the genus of RNA regions encompassed by the claims.

In view of the foregoing, Applicants submit that the specification reasonably conveys to one of skill in the art that Applicants had possession of the claimed invention at the time the application was filed and therefore respectfully requests withdrawal of this rejection.

Claim Rejection – 35 U.S.C. § 112, first paragraph (enablement)

Claims 1-6, 10-18, 20-21, 24, 27, and 30 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a method for reducing seed shattering in a Brassica napus plant while maintaining an agronomically relevant threshability by expressing a gene silencing cassette containing an inverted repeat of a 211 bp fragment from nucleotides 27-239 of SEQ ID NO: 1 driven by a CaMV35S promoter,* does not allegedly reasonably provide enablement for *a method for any oilseed rape plant by expressing any other gene silencing cassette.* Applicants respectfully disagree and traverse this rejection.

Without acquiescing to the correctness of the rejection, Applicants have amended claims 1-2, 15, 24, and 27 and cancelled claims 2-6, 10-14, 18, 20-21, and 30. Furthermore, Applicants provide the following remarks.

The specification describes the manufacture of chimeric genes encoding dsRNA capable of reducing the expression of a gene involved in dehiscence zone and value margin

development and their use in making transgenic *Arabidopsis thaliana* and *Brassica napus* lines comprising these chimeric genes. *See* Specification at Examples 1 and 2.

The specification teaches that dsRNA gene-silencing of the INDEHISCENT gene can decrease pod shatter, while maintaining agronomically relevant threshability. *See* Specification at ¶¶ [0026], [0048], and [0049]. The specification also teaches that the skilled artisan can achieve moderate gene silencing by introducing a dsRNA encoding chimeric gene where the sense and antisense region of the dsRNA exhibit less than 90% homology with the endogenous gene, and preferably within a range of about 60 to 80% homology. *See* Specification at ¶¶ [0026], [0048], and [0049]. This has been demonstrated by introducing a chimeric gene derived from the *Arabidopsis thaliana* IND gene into *Brassica napus* and by performing the reverse experiment (*i.e.*, introducing a dsRNA encoding chimeric gene derived from *Brassica napus* into *Arabidopsis thaliana*). *See* Specification at Example 2, Tables 1 and 2.

It is clear to the skilled artisan that the transgenic *Arabidopsis thaliana* lines where silencing was achieved with a dsRNA encoding chimeric gene being derived from the *Brassica napus* IND sequences exhibited an increased pod shatter resistance, but still could be opened by using moderate pressure forces ("agronomally relevant threshability"). *See* Specification at ¶ [00093]. Thus the specification provides sufficient guidance, including examples, that using dsRNA encoding chimeric genes based upon sequences having about 65% sequence homology to the endogenous gene (*i.e.*, using *Arabidopsis thaliana* IND gene based dsRNA genes in *Brassica napus* or *Brassica napus* IND gene based dsRNA genes in *Arabidopsis thaliana*) will result in a moderate pod shatter resistance. Specification at ¶ [00072]. Therefore, the applicability of the claimed methods are not limited to the exemplified pTCO219 gene silencing vector, but reasonably extrapolated to other plants without undue experimentation.

Further, the specification teaches that dsRNA encoding chimeric genes should not include the common protein motives of genes involved in pod dehiscense such as K-box, MADS box or basic helix-loop-helix (bHLH) domain because domains usually exhibit a higher sequence homology than the overall homology between orthologues from different plant species and result in a higher than desired gene silencing. *See* Specification at ¶ [00059]. For instance, Figure 1 shows the sequence homology in the 3' end of the IND sequences from *Brassica napus* and *Arabidopsis thaliana* which show a high degree of

homology due to the presence of the bHLH domain in the encoded protein. Accordingly, the specification provides ample guidance that would allow the skilled person to extrapolate the exemplified embodiment to the currently claimed methods without undue experimentation.

The Office Action also alleged that it is unclear that pTCO219 would work similarly in other oilseed rape plants as in *Brassica napus* since the specification allegedly does not teach any homologous gene of INDEHISCENT in other oilseed rape plants that might be suppressed. Applicants respectfully disagree.

The two copies of the homologues of the INDEHISCENT gene in *Brassica napus* disclosed in the application are respectively the orthologue of the A and the C subgenome of the *Brassica napus* genome. The two other currently recited oilseed rape species *Brassoca campestris* (amphidiploid BBCC) and *Brassica junceae* (amphidiploid AABB) each share one subgenome with *Brassica napus*, and thus contain at least one corresponding copy of the INDEHISCENT gene. Moreover, the specification teaches that a similar experiment produces similar results in species as distinct as *Arabidopsis thaliana* and *Brassica napus*, clearly providing support for the methods to work in more closely related species such a *Brassica campestris* and *Brassica junceae* without undue experimentation.

Finally, the Office Action alleged that the specification shows that promoter activity affects the outcome of the claimed method and that Applicants failed to teach which combinations of strength of promoter, homology of sequence and length of sequence will yield the desirable results.

Applicants respectfully traverse. The specification teaches moderate gene silencing, achieving the desired effect is obtained either by using a weak promoter (and using a dsRNA completely homologous to the endogenous IND gene) or by using a dsRNA with lower homology to the endogenous IND gene. Specification at ¶ [00049]; Table 1. There is no experimental evidence that the strength of the promoter further influences the moderate gene silencing when using a dsRNA with lower homology to the endogenous IND gene as currently claimed.

Applicants respectfully submit that the specification provides sufficient guidance to the skilled artisan to use dsRNA encoding chimeric genes based on nucleotide sequences of at least 200 nucleotides selected from the nucleotide sequence of the *Arabidopsis thaliana*

IND gene (SEQ ID NO:1) outside of the bHLH encoding region for the methods of reducing pod shatter, while maintaining agronomical relevant threshability as the exemplified by the fragment of 211 nucleotides without undue experimentation.

In view of foregoing, Applicants submit that the specification provides the requisite guidance to enable the full scope of the invention and therefore Applicants respectfully request withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 1-6, 10-18, 20-21, 24, 27, and 30 were rejected under 35 U.S.C. § 103 as being obvious over U.S. Pat. No. 7,135,621 (Yanofsky, *et al.*) ("the '621 patent") in view of Smith, *et al.* (September 21, 2000) Nature **407**: 319-320 ("Smith").

The Office Action asserts that the '621 patent teaches a method of selecting a *Brassica* plant with delayed fruit dehiscence comprising, *inter alia*, introducing into plants a recombinant expression cassette comprising a promoter operably linked to an antisense nucleotide sequence of nucleotides 2765-3361 of SEQ ID NO: 1 (the coding sequence of the bHLH), which represents the coding region of the Arabidopsis INDEHISCENT gene. *See* the '621 patent SEQUENCE LISTING at SEQ ID NO: 1. The Examiner then states that '621 patent does not teach, *inter alia*, an expression cassette comprising a promoter operably linked to an inverted repeat. Rather, the Examiner relies on Smith to support the proposition that "it would have been obvious for a person with ordinary skill in the art to modify the gene silencing vector of Yanofsky et al. by replacing the antisense fragment with an inverted repeat structure according to the teaching of Smith et al." Office Action, page 15. The Office Action asserts that one "skilled in the art would have been motivated to do so given the teachings of Smith et al. that the modifications increase the efficiency of gene silencing compared to antisense construct." *Id.*

Applicants respectfully disagree and traverse this rejection. As an initial matter, Applicants submit that each and every claim limitation is not taught by the '621 patent either alone, or in combination with Smith. For example, claim 1 requires that the "first RNA region comprises a nucleotide sequence of at least 200 consecutive nucleotides of the nucleotide sequence of SEQ ID NO: 1 *other than a bHLH encoding region.*" [emphasis added]. The '621 patent, however, requires the use of a polynucleotide which encodes a polypeptide comprising a bHLH domain. *See, e.g.*, '621 patent at claims 1, 6, 18 and 20;

see also col. 10, lines 26-30 ("In particular, the invention provides methods of delaying or preventing fruit dehiscence by suppressing expression of an bHLH gene such as IND1 in a plant.") Smith does remedy this deficiency.

Applicants also disagree with the Office Action's assertion that one of ordinary skill in the art one "would have been motivated" to modify teachings of the '621 patent with the teachings of Smith. Indeed, the thrust of the present invention is to *moderate* the silencing described by the '621 patent and not to increase the efficiency of such silencing. Accordingly, a person set out to modify the methods described by the '621 patent to obtain a milder silencing of the IND genes, would not turn to the Smith reference which exactly discloses the opposite.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

Claims 1-6, 10-18, 20-21, 24, 27, and 30 have been rejected under 35 U.S.C. § 103 as being obvious over U.S. Patent No. 6,998,517 (Liljegren, *et al.*) ("the '517 patent") in view of Smith, *et al.* (September 21, 2000) Nature **407**: 319-320 ("Smith").

The Office Action alleges that the '517 patent teaches a method of selecting a *Brassica* plant with delayed fruit dehiscence comprising, *inter alia*, introducing into plants a recombinant expression cassette comprising a promoter operably linked to an antisense nucleotide sequence of nucleotides 2765-3361 of SEQ ID NO: 1 (the coding sequence of the bHLH domain), which represents the coding region of the Arabidopsis INDEHISCENT gene. *See* the '517 patent Col. 7, lines 27-41; SEQUENCE LISTING at SEQ ID NO: 1. The Examiner then states that '517 patent does not teach, *inter alia*, an expression cassette comprising a promoter operably linked to an inverted repeat. Rather, the Examiner relies on Smith to support the proposition that "it would have been obvious for a person with ordinary skill in the art to modify the gene silencing vector of Lijegren et al. by replacing the antisense fragment with an inverted repeat structure according to the teaching of Smith et al." Office Action, page 19. The Office Action asserts that one "skilled in the art would have been motivated to do so given the teachings of Smith et al. that the modifications increase the efficiency of gene silencing compared to antisense construct." *Id.*

Applicants respectfully disagree and traverse this rejection. As an initial matter, Applicants submit that each and every claim limitation is not taught by the '517 patent

either alone, or in combination with Smith. For example, claim 1 requires that the "first RNA region comprises a nucleotide sequence of at least 200 consecutive nucleotides of the nucleotide sequence of SEQ ID NO: 1 *other than a bHLH encoding region.*" [emphasis added]. The '517 patent, however, requires the use of a polynucleotide which encodes a polypeptide comprising a bHLH domain. *See, e.g.*, '517 patent at claims 12, 22, and 31; *see also* col. 10, lines 6-10 ("In particular, the invention provides methods of delaying or preventing fruit dehiscence by suppressing expression of an bHLH gene such as IND1 in a plant.") Smith does remedy this deficiency.

Applicants also disagree with the Office Action's assertion that one of ordinary skill in the art one "would have been motivated" to modify teachings of the '517 patent with the teachings of Smith. Indeed, the thrust of the present invention is to *moderate* the silencing described by the '517 patent and not to increase the efficiency of such silencing. Accordingly, a person set out to modify the methods described by the '517 patent to obtain a milder silencing of the IND genes, would not turn to the Smith reference which exactly discloses the opposite.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

Nonstatutory Obviousness-type Double Patenting

Claims 1-6, 10-18, 20-21, 24, 27, and 30 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29-39 of U.S. Patent No. 6,998,517 (Liljegren, *et al.*) ("the '517 patent) in view of Smith, *et al.* (September 21, 2000) Nature 407: 319-320 ("Smith").

The Office Action alleges that the '517 patent teaches a method of selecting a *Brassica* plant with delayed fruit dehiscence comprising, *inter alia*, introducing into plants a recombinant expression cassette comprising a promoter operably linked to an antisense nucleotide sequence of nucleotides 2765-3361 of SEQ ID No: 1 (the coding sequence of the bHLH domain), which represents the coding region of the Arabidopsis INDEHISCENT gene. *See* the '517 patent Col. 7, lines 27-41; SEQUENCE LISTING at SEQ ID NO: 1. The Examiner then states that '517 patent does not teach, *inter alia*, an expression cassette comprising a promoter operably linked to an inverted repeat. Rather, the Examiner relies on Smith to support the proposition that "it would have been obvious for a person with ordinary skill in the art to modify the gene silencing vector of Lijegren et al. by replacing

the antisense fragment with an inverted repeat structure according to the teaching of Smith et al." Office Action, page 19. The Office Action asserts that one "skilled in the art would have been motivated to do so given the teachings of Smith et al. that the modifications increase the efficiency of gene silencing compared to antisense construct." *Id.*

Applicants respectfully disagree and traverse this rejection. As an initial matter, Applicants submit that each and every claim limitation is not taught by the '517 patent either alone, or in combination with Smith. For example, claim 1 requires that the "first RNA region comprises a nucleotide sequence of at least 200 consecutive nucleotides of the nucleotide sequence of SEQ ID NO: 1 *other than a bHLH encoding region*." [emphasis added]. The '517 patent, however, requires the use of a polynucleotide which encodes a polypeptide comprising a bHLH domain. *See, e.g.*, '517 patent at claims 12, 22, and 31; *see also* col. 10, lines 6-10 ("In particular, the invention provides methods of delaying or preventing fruit dehiscence by suppressing expression of an bHLH gene such as IND1 in a plant.") Smith does remedy this deficiency.

Applicants also disagree with the Office Action's assertion that one of ordinary skill in the art one "would have been motivated" to modify teachings of the '517 patent with the teachings of Smith. Indeed, the thrust of the present invention is to *moderate* the silencing described by the '517 patent and not to increase the efficiency of such silencing. Accordingly, a person set out to modify the methods described by the '517 patent to obtain a milder silencing of the IND genes, would not turn to the Smith reference which exactly discloses the opposite.

Finally, claims 22 (upon which claim 29 depends) and 31 (upon which claims 32-39 depend) expressly require that the polynucleotide comprises nucleotides 2765-3361 which encodes the bHLH domain. In contrast, claim 1 expressly excludes a nucleotide encoding a bHLH domain. Therefore, instant claims 1-6, 10-18, 20-21, 24, 27, and 30 are not coextensive with claims 29-39 of the '517 patent.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

Claims 1-6, 10-18, 20-21, 24, 27, and 30 have been rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-28 of US patent 7,135,621 (Yanofsky, *et al.*) ("the '621 patent") in view of Smith, *et al.* (September 21, 2000) Nature 407: 319-320 ("Smith").

The Office Action asserts that the '621 patent teaches a method of selecting a *Brassica* plant with delayed fruit dehiscence comprising, *inter alia*, introducing into plants a recombinant expression cassette comprising a promoter operably linked to an antisense nucleotide sequence of nucleotides 2765-3361 of SEQ ID No: 1 (the coding sequence of the bHLH), which represents the coding region of the Arabidopsis INDEHISCENT gene. *See* the '621 patent SEQUENCE LISTING at SEQ ID NO: 1. The Examiner then states that '621 patent does not teach, *inter alia*, an expression cassette comprising a promoter operably linked to an inverted repeat. Rather, the Examiner relies on Smith to support the proposition that "it would have been obvious for a person with ordinary skill in the art to modify the gene silencing vector of Yanofsky et al. by replacing the antisense fragment with an inverted repeat structure according to the teaching of Smith et al." Office Action, page 15. The Office Action asserts that one "skilled in the art would have been motivated to do so given the teachings of Smith et al. that the modifications increase the efficiency of gene silencing compared to antisense construct." *Id.*

Applicants respectfully disagree and traverse this rejection. As an initial matter, Applicants submit that each and every claim limitation is not taught by the '621 patent either alone, or in combination with Smith. For example, claim 1 requires that the "first RNA region comprises a nucleotide sequence of at least 200 consecutive nucleotides of the nucleotide sequence of SEQ ID NO: 1 *other than a bHLH encoding region.*" [emphasis added]. The '621 patent, however, requires the use of a polynucleotide which encodes a polypeptide comprising a bHLH domain. *See, e.g.*, '621 patent at claims 1, 6, 18 and 20; *see also* col. 10, lines 26-30 ("In particular, the invention provides methods of delaying or preventing fruit dehiscence by suppressing expression of an bHLH gene such as IND1 in a plant.") Smith does remedy this deficiency.

Applicants also disagree with the Office Action's assertion that one of ordinary skill in the art one "would have been motivated" to modify teachings of the '621 patent with the teachings of Smith. Indeed, the thrust of the present invention is to *moderate* the silencing described by the '621 patent and not to increase the efficiency of such silencing.

Accordingly, a person set out to modify the methods described by the '621 patent to obtain a milder silencing of the IND genes, would not turn to the Smith reference which exactly discloses the opposite.

Finally, claims 6 (upon which claims 7-17 depend), 18 (upon which claim 19 depends), and claim 20 (upon which claims 21-28 depend) expressly require that the polynucleotide comprise a basic helix-loop-helix domain (i.e., nucleotides 2765-3361). In contrast, claim 1 expressly excludes a nucleotide encoding a bHLH domain. Therefore, instant claims 1-6, 10-18, 20-21, 24, 27, and 30 are not coextensive with claims 6-28 of the '621 patent.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any issues remain after consideration of this Response, the Examiner is invited to contact the Applicant's undersigned representative to discuss and resolve such issues.

It is believed that no other fees are required for entry of these remarks, but should any fees be necessary, the Commissioner is authorized to charge such fees to **Deposit Account No. 50-0206.**

Respectfully submitted,

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